ORIGINAL ARTICLE

Korean J Intern Med 2024;39:137-147
https://doi.org/10.3904/kjim.2023.036

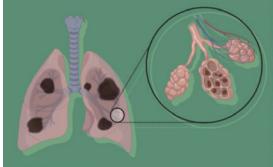
Sex differences in chronic obstructive pulmonary disease characteristics: the Korea National Health and Nutrition Examination Survey 2007–2018

Moon Seong Baek[1,*], Haegwang Shin[1,*], Kang-Mo Gu[1], Hae In Jung[1], Won Young Kim[1], Jae-Woo Jung[1], Jong-Wook Shin[1], Sun-Young Jung[2], and Jae-Yeol Kim[1]

[1]Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul; [2]College of Pharmacy, Chung-Ang University, Seoul, Korea.

*These authors contributed equally to this manuscript.

Sex differences in COPD characteristics: the Korea National Health and Nutrition Examination Survey 2007-2018



	Age	Smoker	Household income	Asthma	Overall malignancy	Lung cancer
Men	62.3±0.2 years	89%	Higher	11.6%	5.4%	0.9%
Women	64.1±0.4 years	14%	Lower	25.5%	6.3%	0.1%

Conclusion Females with COPD had a lower smoking rate, household income, and lung cancer prevalence than males with COPD. More active COPD screening is needed for women of low socioeconomic status, even if they do not smoke.

Background/Aims: Chronic obstructive pulmonary disease (COPD) is less prevalent in females than males, but it affects mortality in females. There may be sex differences in the clinical characteristics of COPD.

Methods: We analyzed the Korea National Health and Nutrition Examination Survey dataset from 2007 to 2018. We compared the clinical characteristics and comorbidities in subjects with COPD according to sex. We adjusted the multivariate logistic regression of lung cancer prevalence according to COPD and sex by age and smoking amount.

Results: Females with COPD tended to be older than males with COPD (64.1 ± 0.4 yr vs. 62.3 ± 0.2 yr, respectively, $p < 0.001$). Approximately 89% of males with COPD had a smoking history, while 86% of females with COPD were non-smokers ($p < 0.001$).

pISSN 1226-3303
eISSN 2005-6648
http://www.kjim.org

Household income was lower ($p < 0.001$) and asthma and overall malignancy were more prevalent in females with COPD than males with COPD (25.5 vs. 11.6%, respectively, $p < 0.001$; (6.3 vs. 5.4%, respectively, $p < 0.001$). However, lung cancer was more common in males with COPD than females with COPD (0.9 vs. 0.1%, respectively, $p < 0.001$). Lung cancer prevalence increased in males with moderate COPD compared to subjects without COPD (OR, 4.409; 95% CI, 1.741–9.419).
Conclusions: Females with COPD had a lower smoking rate, household income, and lung cancer prevalence than males with COPD. More active COPD screening is needed for women of low socioeconomic status, even if they do not smoke.

Keywords: Pulmonary disease, chronic obstructive; Sex; Smoking; Lung neoplasm

INTRODUCTION

Globally, chronic obstructive pulmonary disease (COPD) is the third leading cause of death [1]. Approximately 3.2 million people died from COPD in 2015 [2], and its prevalence and mortality rate is increasing [1,2]. COPD is characterized by persistent respiratory symptoms and airflow limitation [3], which manifest the airway and/or alveolar abnormalities typically caused by exposure to noxious particles or gases. Cigarette smoking is the most important risk factor for COPD, but factors such as indoor air pollution, work environment exposure, and passive smoking also contribute to its development [4,5]. Average smoking exposure is associated with an increased risk of COPD [6]. There is a dose-response relationship between smoking and a decline in lung function [5,7]; however, this relationship varies by individual. A substantial proportion of patients with COPD have never smoked [8], while others have minimal to no symptoms despite a history of heavy smoking [9].

A recent systematic review and meta-analysis reported that a COPD prevalence of 9.2% in men and 6.2% in women [10]. However, COPD is gradually becoming an important factor affecting women's mortality and quality of life [11]. In general, the smoking rate is lower in women than men [12,13], but women generally experience a greater decline in lung function than men at the same smoking exposure. There may be sex differences in lung damage susceptibility associated with cigarette smoking [14], and women who have never smoked may have prolonged exposure to organic dust [8]. Therefore, the phenotypes of women with COPD may differ from those of men with COPD, which has not been evaluated on a nationwide scale. In the present study, we aimed to identify the difference in baseline characteristics and comorbidities, including lung cancer, in patients with COPD according to sex using a Korean nationwide database.

METHODS

Korea National Health and Nutrition Examination Survey

The Korea National Health and Nutrition Examination Survey (KNHANES) is an ongoing, population-based, nationwide, cross-sectional survey conducted annually by the Korea Disease Control and Prevention Agency (KDCA), which has been assessing the health and nutritional status of Koreans since 1998. The KNHANES represents the general Korean population because it involves a stratified, multistage, clustered sampling based on national census data [15]. Health trends can be deduced by merging yearly data. The KDCA institutional review board approved all KNHANES survey protocols (2015-01-02-6C). The questionnaire and dataset had guidelines for calculating a health-related index indicated by the KDCA (available at https://knhanes.kdca.go.kr/knhanes/main.do). We evaluated data from 2007 to 2018 as KNHANES has used spirometry to measure pulmonary function tests (PFTs) since 2007.

The study protocol was reviewed and approved by the Institutional Review Board of Chung-Ang University Hospital (approval no. 2312-004-19500). The requirement for informed consent was waived as all subjects were de-identified.

COPD diagnosis

PFT was performed on subjects older than 40 years of age during the KNHANES health examination by well-trained technicians according to the guidelines [16,17]. Because post-bronchodilator PFT was not available in the KNHANES dataset, we used pre-bronchodilator PFT findings. A diagnosis of COPD was established based on PFT parameters using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [3]. Subjects with a ratio of forced

https://doi.org/10.3904/kjim.2023.036

expiratory volume in one second (FEV1)/forced vital capacity (FVC) < 0.7 were determined to have COPD. Airflow limitation severity was classified according to the GOLD criteria, as follows: GOLD I (mild): FEV1 ≥ 80%; GOLD II (moderate): 50% ≤ FEV1 < 80%; GOLD III (severe): 30% ≤ FEV1 < 50%; GOLD IV (very severe): FEV1 < 30% predicted [3].

Demographic data

We collected sociodemographic data, such as age, sex, body mass index (BMI), waist circumference, household income level, educational level, and marital status. Household income was divided into four quartiles: the lowest quartile, lower-middle quartile, upper-middle quartile, and highest quartile. Educational levels were divided according to graduation level (elementary school, middle school, high school, and college or more). Marital status was classified as not married, married, married but spouse deceased, and divorced). Comorbidities included a self-reported physician diagnosis of pulmonary tuberculosis, asthma, hypertension, diabetes, chronic renal disease, liver cirrhosis, and malignancies, including lung cancer. We obtained urinary cotinine and laboratory results, including white blood cells, hemoglobin, alanine aminotransferase, creatinine, fasting glucose, glycated hemoglobin levels, and lipid profiles.

Smoking status

All subjects were asked if they had smoked at least 100 cigarettes (five packs) in their lifetime. Those who answered 'no' were categorized as 'non-smokers.' Subjects who indicated that they do not currently smoke but have smoked more than 100 cigarettes were categorized as 'ex-smokers,' and those who answered 'yes' were defined as 'current smokers.'

Statistical analysis

Continuous variables are presented as means ± standard deviations and categorical data as frequencies and percentiles. We performed an intergroup comparison of demographic data and airflow obstruction severity between men and women with COPD by t-test and an intergroup comparison of categorical data between men and women with COPD with the chi-square test. Major comorbidities included pulmonary tuberculosis, asthma, hypertension, diabetes, chronic renal disease, liver cirrhosis, and malignancies, including lung cancer. We adjusted the multivariate logistic regression of the lung cancer prevalence according to COPD severity by age and smoking amount, and then calculated the odds ratio (OR) and 95% confidence intervals (CIs). The results were analyzed using SPSS statistics complex samples procedures (version 26.0; IBM Corp., Armonk, NY, USA). All proportion estimates were weighted to the general Korean population using longitudinal weights supplied by the KDCA. We conducted two-tailed analyses, and p values lower than 0.05 were considered significant.

RESULTS

Study population

The KNHANES data included 97,622 people during the study period (Fig. 1). We excluded 45,013 who were < 40 years old. Of the remaining 52,609 subjects, we excluded 14,362 who did not have spirometry results or who were missing spirometry values. We analyzed 38,247 subjects aged ≥ 40 years who had spirometry results. Among them, 5,413 (14.2%) met the COPD criteria of FEV1/FVC < 0.7 on PFT. In total, 23.4% of males had COPD (3,921 out of 16,782) and 7.0% of females had COPD (1,492 out of 21,465) (Fig. 1).

Comparison of clinical characteristics in males with and without COPD

Males with COPD were older than those without COPD (62.3 ± 0.2 yr vs. 52.5 ± 0.1 yr, respectively, $p < 0.001$) and

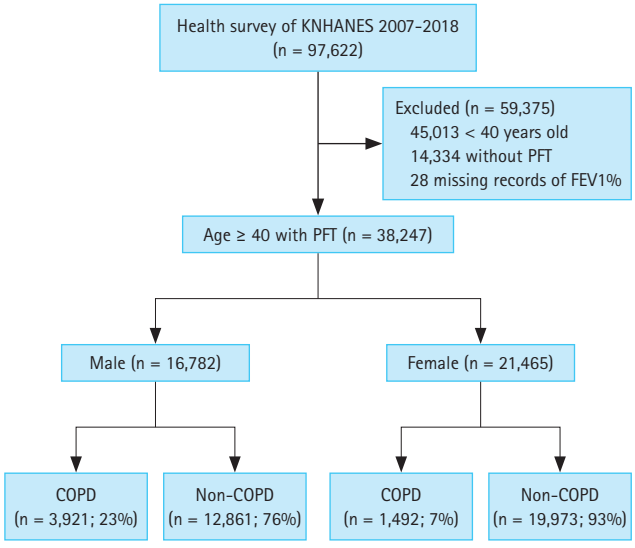


Figure 1. Flow diagram of the study population. COPD, chronic obstructive pulmonary disease; KNHANES, Korea National Health and Nutrition Examination Survey; PFT, pulmonary function test.

Table 1. The clinical characteristics of male subjects with and without COPD

Characteristic	Non-COPD (n = 12,861)	COPD (n = 3,921)	*p* value[a)]
Age (yr)	52.5 ± 0.1	62.3 ± 0.2	< 0.001
BMI (kg/m^2)	24.6 ± 0.3	23.8 ± 0.6	< 0.001
Waist circumference (cm)	86.3 ± 0.9	86.0 ± 0.16	< 0.001
Smoking status (%)			< 0.001
Non-smoker	17.2	10.6	
Ex-smoker	34.0	37.2	
Current smoker	48.8	52.2	
Smoking amounts (pack year)	14.1 ± 0.2	20.9 ± 0.4	< 0.001
Urine cotinine (ng/mL)	579.4 ± 12.8	651.2 ± 25.5	< 0.001
Pulmonary function test (%)			
FVC	90.8 ± 0.1	89.4 ± 0.3	< 0.001
FEV1	91.5 ± 0.1	76.6 ± 0.3	< 0.001
FEV1/FVC	78.8 ± 0.1	62.9 ± 0.1	< 0.001
Household income (%)			< 0.001
Lowest quartile	11.5	27.1	
Lower middle quartile	23.8	27.6	
Upper middle quartile	29.5	23.7	
Highest quartile	35.2	21.6	
Marital status (%)			< 0.001
Single	4.6	1.9	
Married	89.9	90.0	
Widowed	1.2	3.3	
Divorced	4.3	4.7	
Education (%)			< 0.001
Elementary school	12.7	33.1	
Middle school	13.5	18.8	
High school	36.0	29.0	
College or more	37.7	19.1	
Laboratory findings			
WBC (× 10^3/uL)	6.6 ± 0.0	6.8 ± 0.0	< 0.001
Hemoglobin (/uL)	15.3 ± 0.0	15.0 ± 0.0	< 0.001
ALT (IU/L)	28.0 ± 0.3	23.9 ± 0.3	< 0.001
Creatinine (mg/dL)	1.0 ± 0.0	1.0 ± 0.0	< 0.001
Fasting glucose (mg/dL)	105.1 ± 0.3	105.1 ± 0.5	< 0.001
HbA1c (%)	6.0 ± 0.0	6.0 ± 0.0	< 0.001
Triglyceride (mg/dL)	177.7 ± 1.7	163.2 ± 2.8	< 0.001
HDL-cholesterol (mg/dL)	46.1 ± 0.1	45.8 ± 0.2	< 0.001
LDL-cholesterol (mg/dL)	116.6 ± 0.7	111.2 ± 1.2	< 0.001
Total cholesterol (mg/dL)	194.0 ± 0.4	186.6 ± 0.7	< 0.001

Values are presented as mean ± standard error or percentage only.
ALT, alanine aminotransferase; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WBC, white blood cell.
[a)]Results were adjusted for sampling weight.

https://doi.org/10.3904/kjim.2023.036

Table 2. The clinical characteristics of female subjects with and without COPD

Characteristic	Non-COPD (n = 19,973)	COPD (n = 1,492)	*p* value[a)]
Age (yr)	54.9 ± 0.1	64.1 ± 0.4	< 0.001
BMI (kg/m^2)	24.1 ± 0.0	23.5 ± 0.1	< 0.001
Waist circumference (cm)	80.7 ± 0.1	81.0 ± 0.3	< 0.001
Smoking status (%)			< 0.001
Non-smoker	91.5	85.7	
Ex-smoker	3.0	3.6	
Current smoker	5.5	10.7	
Smoking amounts (pack year)	0.6 ± 0.0	1.6 ± 0.2	< 0.001
Urine cotinine (ng/mL)	76.5 ± 3.9	87.9 ± 10.7	< 0.001
Pulmonary function test (%)			
FVC	92.8 ± 0.1	90.3 ± 0.5	< 0.001
FEV1	93.7 ± 0.1	77.0 ± 0.5	< 0.001
FEV1/FVC	80.5 ± 0.0	64.8 ± 0.2	< 0.001
Household income (%)			< 0.001
Lowest quartile	19.0	40.4	
Lower middle quartile	25.6	24.1	
Upper middle quartile	26.0	19.0	
Highest quartile	29.3	16.6	
Marital status (%)			< 0.001
Single	1.5	0.6	
Married	79.9	60.0	
Widowed	13.2	33.6	
Divorced	5.4	5.8	
Education (%)			< 0.001
Elementary school	30.4	58.7	
Middle school	15.0	13.8	
High school	34.8	18.8	
College or more	19.8	8.7	
Laboratory findings			
WBC (× 10^3/uL)	5.8 ± 0.0	6.0 ± 0.1	< 0.001
Hemoglobin (/uL)	13.1 ± 0.0	13.1 ± 0.0	< 0.001
ALT (IU/L)	19.6 ± 0.1	18.5 ± 0.3	< 0.001
Creatinine (mg/dL)	0.7 ± 0.0	0.8 ± 0.0	< 0.001
Fasting glucose (mg/dL)	99.1 ± 0.2	100.6 ± 0.7	< 0.001
HbA1c (%)	5.8 ± 0.0	6.0 ± 0.0	< 0.001
Triglyceride (mg/dL)	125.6 ± 0.9	127.8 ± 2.3	< 0.001
HDL-cholesterol (mg/dL)	52.0 ± 0.1	50.7 ± 0.4	< 0.001
LDL-cholesterol (mg/dL)	120.3 ± 0.6	119.4 ± 2.4	< 0.001
Total cholesterol (mg/dL)	197.8 ± 0.3	196.2 ± 1.2	< 0.001

Values are presented as mean ± standard error or percentage only.

ALT, alanine aminotransferase; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; WBC, white blood cell.

[a)]Results were adjusted for sampling weight.

Table 3. Comparisons of clinical characteristics in subjects with COPD according to sex

Characteristic	Male COPD (n = 3,921)	Female COPD (n = 1,492)	*p* value[a]
Age (yr)	62.3 ± 0.2	64.1 ± 0.4	< 0.001
BMI (kg/m^2)	23.8 ± 0.1	23.5 ± 0.1	< 0.001
Smoking status (%)			< 0.001
Non-smoker	10.6	85.7	
Ex-smoker	37.2	3.6	
Current smoker	52.2	10.7	
Smoking amounts (pack year)	20.9 ± 0.4	1.6 ± 0.2	< 0.001
Urine cotinine (ng/mL)	651.2 ± 25.5	87.9 ± 10.7	< 0.001
Secondhand smoke	44.7	37.3	< 0.001
Workplace	33.4	26.1	< 0.001
Home	4.5	6.6	< 0.001
Pulmonary function test (%)			
FVC	89.4 ± 0.3	90.3 ± 0.5	< 0.001
FEV1	76.6 ± 0.3	77.0 ± 0.5	< 0.001
FEV1/FVC	62.9 ± 0.1	64.8 ± 0.2	< 0.001
COPD stage (%)[b]			0.046
GOLD I	44.4	42.7	
GOLD II	49.9	51.7	
GOLD III	5.0	5.3	
GOLD IV	0.7	0.3	
Household income (%)			< 0.001
Lowest quartile	27.1	40.4	
Lower middle quartile	27.6	24.1	
Upper middle quartile	23.7	19.0	
Highest quartile	21.6	16.6	
Comorbidities (%)			
History of pulmonary tuberculosis	19.5	19.6	< 0.001
Asthma	11.6	25.5	< 0.001
Hypertension	50.6	54.0	< 0.001
Diabetes	23.7	20.8	< 0.001
Chronic renal disease	1.2	0.6	< 0.001
Liver cirrhosis	1.5	0.1	< 0.001
Malignancy	5.4	6.3	< 0.001
Lung cancer	0.9	0.1	< 0.001
Stomach cancer	3.3	2.0	< 0.001
Hepatocellular carcinoma	0.4	0.2	0.185
Colon cancer	2.2	1.1	< 0.001

Values are presented as mean ± standard error or percentage only.
BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease.
[a]Results were adjusted for sampling weight.
[b]The GOLD system categorizes airflow limitation into the following stages: GOLD I - mild: FEV1 ≥ 80% predicted; GOLD II - moderate: 50% ≤ FEV1 < 80% predicted; GOLD III - severe: 30% ≤ FEV1 < 50% predicted; GOLD IV - very severe: FEV1 < 30% predicted.

https://doi.org/10.3904/kjim.2023.036

had a lower BMI (23.8 ± 0.6 kg/m^2 vs. 24.6 ± 0.3 kg/m^2, respectively, $p < 0.001$) (Table 1). Males with COPD were more likely to have a smoking history (89.4 vs. 82.8%, respectively, $p < 0.001$) and higher urinary cotinine levels (651.2 ± 25.5 ng/mL vs. 579.4 ± 12.8 ng/mL, respectively, $p < 0.001$) than those without COPD. Males with COPD had lower PFT values, including FVC (%), FEV1 (%), and FEV1/FVC, and lower household income and education levels than in those without COPD.

Comparison of clinical characteristics in females with and without COPD

The females COPD group was older (64.1 ± 0.1 yr vs. 54.9 ± 0.1 yr, respectively, $p < 0.001$) and had a lower BMI (23.5 ± 0.1 kg/m^2 vs. 24.1 ± 0.0 kg/m^2, respectively, $p < 0.001$) than the non-COPD group (Table 2). The female COPD group had a higher smoking history (14.3 vs. 8.5%, respectively, $p < 0.001$) and higher urinary cotinine levels (87.9 ± 10.7 ng/mL vs. 76.5 ± 3.9 ng/mL, respectively, $p < 0.001$) than the non-COPD group. Females with COPD had lower spirometry values, such as FVC (%), FEV1 (%), and FEV1/FVC, and lower household income and education levels than those without COPD. There were more widowed or divorced subjects in the COPD group than the non-COPD group (39.4 vs. 18.6%, respectively, $p < 0.001$).

Table 4. The prevalence of lung cancer according to the presence of COPD and sex[a)]

Variable	Lung cancer (-)	Lung cancer (+)	OR (95% CI)
Total[b)]			
No COPD	99.9	0.1	Reference
COPD	99.3	0.7	2.033 (1.112–3.715)
Male[c)]			
No COPD	99.8	0.2	Reference
COPD	99.1	0.9	2.574 (1.214–3.715)
Female[c)]			
No COPD	99.9	0.1	Reference
COPD	99.9	0.1	0.519 (0.295–0.910)

Values are presented as percentage only.
CI, confidence interval; COPD, chronic obstructive pulmonary disease; OR, odds ratio.
[a)]Results were adjusted for sampling weight.
[b)]Adjusted by age, sex, and pack-years.
[c)]Adjusted by age and pack-years.

Comparison of clinical characteristics in subjects with COPD according to sex

The female COPD group was older than the male COPD group (64.1 ± 0.4 yr vs. 62.3 ± 0.2 yr, respectively, $p < 0.001$) (Table 3). In total, 89.4% of the male COPD group had a smoking history, however, 85.7% of females with COPD were non-smokers ($p < 0.001$). Urinary cotinine levels were higher in males than females (651.2 ± 25.5 ng/mL vs. 87.9 ± 10.7 ng/mL, respectively, $p < 0.001$). Overall rates of secondhand smoke and exposure at the workplace were higher in the male COPD group compared to the female COPD group (44.7 vs. 37.3%, respectively, $p < 0.001$; and 33.4 vs. 26.1%, respectively, $p < 0.001$); however, exposure at home was higher in females with COPD compared to males with COPD (6.6 vs. 4.5%, respectively, $p < 0.001$).

Approximately 5.7% of males with COPD and 5.6% of females with COPD were classified as GOLD levels III and IV ($p = 0.046$). Household income was lower in females with COPD than in males with COPD: 64.5% of females and 54.7% of males were in the lowest and lower middle household income quartiles ($p < 0.001$). In terms of comorbidities, asthma was more prevalent in the female COPD group than in the male COPD group (25.5 vs. 11.6%, respectively, $p < 0.001$). A higher prevalence of overall malignancy was observed in females than males (6.3 vs. 5.4%, respectively, $p < 0.001$); however, lung cancer was more common in the male COPD group than the female COPD group (0.9 vs. 0.1%, respectively, $p < 0.001$).

The association between lung cancer and COPD according to sex

Lung cancer was more common in those with COPD than in those without COPD (OR, 2.033; 95% CI, 1.112–3.715) (Table 4). There was a difference in lung cancer prevalence according to sex. In males, lung cancer was more common in the COPD group than the non-COPD group (OR, 2.574; 95% CI, 1.214–3.715). However, in females, lung cancer was more common in the non-COPD group than the COPD group (OR, 0.519; 95% CI, 0.295–0.910).

Compared to the non-COPD group, the prevalence of lung cancer increased in those with moderate COPD (GOLD II), all subjects (OR, 3.300; 95% CI, 1.642–6.629), and males with COPD (OR, 4.409; 95% CI, 1.741–9.419). However, the ORs for lung cancer were not high in the mild COPD (GOLD I) and severe COPD (GOLD III and IV) groups (Table 5). The relationship between lung cancer and COPD severity is

Table 5. ORs for lung cancer according to COPD severity and sex[a)]

Variable	Lung cancer (-)	Lung cancer (+)	OR (95% CI)
Total[b)]			
Non-COPD	87.7	55.4	Reference
GOLD I	5.7	6.8	0.789 (0.277–2.249)
GOLD II	6.0	32.8	3.300 (1.642–6.629)
GOLD III and IV	0.7	4.9	3.872 (0.759–19.766)
Male[c)]			
Non-COPD	81.3	42.4	Reference
GOLD I	8.6	9.1	1.044 (0.344–3.167)
GOLD II	9.1	42.0	4.409 (1.741–9.419)
GOLD III and IV	1.0	6.6	4.793 (0.870–26.408)
Female[c)]			
Non-COPD	93.9	94.2	Reference
GOLD I	2.9	0	-
GOLD II	2.9	5.8	1.260 (1.260–1.260)
GOLD III and IV	0.3	0	-

Values are presented as percentage only.
CI, confidence interval; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; OR, odds ratio.
[a)]Results were adjusted for sampling weight.
[b)]Adjusted by age, sex, and pack-years.
[c)]Adjusted by age and pack-years.

unclear in females because there were no lung cancer patients with COPD GOLD levels of I, III, and IV.

DISCUSSION

This study compared subjects with and without COPD according to sex. In both males and females, those with COPD were older and had lower household income and educational levels than those without COPD. Smokers and those with a high urinary cotinine level were also more prevalent in the COPD group. Furthermore, several differences in patients with COPD according to sex were noted: males with COPD were associated with a smoking history and lung cancer, while females with COPD had a lower household income and a higher prevalence of asthma.

There are some sex differences in patients with COPD. Females with COPD were less likely to smoke and had lower education and income levels than males with COPD [18,19]. According to Kanervisto et al. [20], subjects with a lower educational level had a 1.8 (95% CI, 1.2–2.6) times higher risk of COPD than those with a higher educational level. Socioeconomic status is also an important risk factor for COPD. According to nationwide data from China, subjects with a low income had a 1.64 ($p < 0.001$) times higher COPD risk than those with a high income, particularly in rural areas [21]. Furthermore, socioeconomic and educational levels are inversely associated with smoking prevalence.

A meta-analysis from Latin America revealed that low income was associated with a 1.62 (95% CI, 1.34–1.96) times higher smoking prevalence than a high income [22]. Kim et al. [23] reported that the risk of smoking was 1.65 (95% CI, 1.44–1.88) for men and 1.90 (95% CI, 1.14–3.16) for women who graduated from middle school or lower than those who graduated from high school or higher. COPD is more frequently underdiagnosed in women than in men [24]. Therefore, more active COPD screening may be needed in women with a low socioeconomic status.

Considering women with COPD have a smoking prevalence as low as 15%, other factors such as secondhand smoke [25] or household air pollution [5,26,27] exposure may contribute to an increased COPD risk. In our study, although

https://doi.org/10.3904/kjim.2023.036

the prevalence of secondhand smoke exposure was higher in men, women were more likely to be exposed to smoke in the home. Furthermore, the overall prevalence of secondhand smoke in females was approximately 37%. Secondhand smoke is a significant risk factor for COPD (OR, 3.80; 95% CI, 1.29–11.2) [25]. Household air pollution from biomass fuels, coal, and kerosene burned in open fires, primitive stoves, and lamps are major risk factors for COPD, particularly for women [5,26,27]. Although household air pollution is a common risk factor for COPD in developing countries, there are still many people with COPD who have a history of exposure to firewood or briquettes in Korea [28]. Korean women are more often in charge of household chores, such as cooking, than men. Household air pollution is a major risk factor for Korean non-smoking females with COPD.

One notable finding in our study is that the prevalence of lung cancer was higher in men with COPD than in those without COPD, but not in females. Smoking is a well-known independent risk factor for lung cancer [29]. Therefore, the smoking exposure of female patients with COPD may have influenced the difference in lung cancer prevalence between men and women with COPD. Another possible explanation for the differences in lung cancer prevalence between men and women is that COPD prevalence differs by sex. COPD increases oxidative stress and damages DNA [30,31]. However, according to a recent large-scale study in Korea, there may be an increased prevalence of lung cancer in those with COPD, even in non-smokers [32]. Furthermore, Nagasaka et al. [33] reported that females with COPD were 1.64 times more likely to develop lung cancer than those without COPD. Lung cancer in women has increased worldwide [30], and secondhand smoke [34] or wood smoke exposure [35] may contribute to the development of lung cancer in women. Therefore, caution is warranted in interpreting our results to indicate a relationship between lung cancer and COPD in women.

Another notable finding was that the prevalence of lung cancer increased in men with moderate COPD. However, there was insufficient evidence to determine this relationship in women. There are conflicting findings on COPD severity and lung cancer prevalence [36-38]. Mannino et al. [36] reported that patients with moderate-to-severe COPD had a 2.8 (95% CI, 1.8–4.4) times higher prevalence of lung cancer. A Cox regression analysis by de Torres et al. [37] showed that GOLD stages I and II are risk factors for lung cancer, but GOLD stages III and IV are not. However, this study included a small number of patients with lung cancer in stage GOLD IV. There may be an increased risk of lung cancer due to impaired clearance of carcinogens and inflammation-related factors with worsening lung function [39]. This relationship may be statistically insignificant because there were few women with lung cancer in our study population. Therefore, further research is warranted.

This study has several limitations. First, airway reversibility results were not available for the COPD diagnosis, as a bronchodilator was not used in the lung function test. Therefore, patients with diseases involving airway reversibility, such as asthma, may have been included in the COPD patient group. Moreover, in our study, the female COPD group included a small number of individuals with lung cancer. Therefore, COPD's contribution to lung cancer development may have been underestimated in females. Second, we did not determine inhalant or steroid use history, which may have impacted disease staging or caused us to incorrectly classify patients with COPD in the normal group during the diagnostic process. Third, it is difficult to evaluate COPD risk factors other than smoking history because we did not evaluate lung damage due to occupational hazards, environment, and biomass smoke. Fourth, we assessed comorbid diseases, educational background, and income through a self-questionnaire, so reliability may vary by the respondent. Despite these limitations, this study is meaningful in that it investigated the differences between men and women with COPD in a large population.

In conclusion, males with COPD were associated with a smoking history and lung cancer, while females with COPD had a lower smoking rate and household income levels. This study showed that people with COPD demonstrated varying phenotypes according to sex. Due to these differences, COPD may be more underdiagnosed in women than in men. More active COPD screening and management are needed in women of low socioeconomic status, even in non-smokers.

KEY MESSAGE

1. Females with COPD had a lower smoking rate, household income, and a lower prevalence of lung cancer than males with COPD.
2. More active COPD screening and management are needed for women of low socioeconomic status, even if they do not smoke.

REFERENCES

1. Christenson SA, Smith BM, Bafadhel M, Putcha N. Chronic obstructive pulmonary disease. Lancet 2022;399:2227-2242.
2. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet Respir Med 2017;5:691-706.
3. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: 2020 report [Internet]. GOLD, c2020 [cited Dec 16, 2022]. Available from: https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf.
4. Oh YM, Bhome AB, Boonsawat W, et al. Characteristics of stable chronic obstructive pulmonary disease patients in the pulmonology clinics of seven Asian cities. Int J Chron Obstruct Pulmon Dis 2013;8:31-39.
5. Tan WC, Sin DD, Bourbeau J, et al.; CanCOLD Collaborative Research Group. Characteristics of COPD in never-smokers and ever-smokers in the general population: results from the CanCOLD study. Thorax 2015;70:822-829.
6. Dai X, Gil GF, Reitsma MB, et al. Health effects associated with smoking: a Burden of Proof study. Nat Med 2022;28:2045-2055.
7. Leem AY, Park B, Kim YS, Chang J, Won S, Jung JY. Longitudinal decline in lung function: a community-based cohort study in Korea. Sci Rep 2019;9:13614.
8. Lamprecht B, McBurnie MA, Vollmer WM, et al.; BOLD Collaborative Research Group. COPD in never smokers: results from the population-based burden of obstructive lung disease study. Chest 2011;139:752-763.
9. Rennard SI, Vestbo J. COPD: the dangerous underestimate of 15%. Lancet 2006;367:1216-1219.
10. Ntritsos G, Franek J, Belbasis L, et al. Gender-specific estimates of COPD prevalence: a systematic review and meta-analysis. Int J Chron Obstruct Pulmon Dis 2018;13:1507-1514.
11. Gut-Gobert C, Cavaillès A, Dixmier A, et al. Women and COPD: do we need more evidence? Eur Respir Rev 2019;28:180055.
12. Kim JY. Directions and challenges in smoking cessation treatment. Tuberc Respir Dis (Seoul) 2020;83(Supple 1):S1-S5.
13. Jeon J, Holford TR, Levy DT, et al. Smoking and lung cancer mortality in the United States from 2015 to 2065: a comparative modeling approach. Ann Intern Med 2018;169:684-693.
14. Sørheim IC, Johannessen A, Gulsvik A, Bakke PS, Silverman EK, DeMeo DL. Gender differences in COPD: are women more susceptible to smoking effects than men? Thorax 2010;65:480-485.
15. Kweon S, Kim Y, Jang MJ, et al. Data resource profile: the Korea National Health and Nutrition Examination Survey (KNHANES). Int J Epidemiol 2014;43:69-77.
16. Graham BL, Steenbruggen I, Miller MR, et al. Standardization of spirometry 2019 update. An official American Thoracic Society and European Respiratory Society technical statement. Am J Respir Crit Care Med 2019;200:e70-e88.
17. Korea Disease Control and Prevention Agency. Quality control program of spirometry at the seventh KNHANES [Internet]. Osong: Korea Disease Control and Prevention Agency, c2017 [cited Aug 18, 2023]. Available from: https://www.prism.go.kr/homepage/entire/researchDetail.do?researchId=1351000-201700231&menuNo=I0000002.
18. Jia G, Lu M, Wu R, Chen Y, Yao W. Gender difference on the knowledge, attitude, and practice of COPD diagnosis and treatment: a national, multicenter, cross-sectional survey in China. Int J Chron Obstruct Pulmon Dis 2018;13:3269-3280.
19. Lopez Varela MV, Montes de Oca M, Halbert RJ, et al.; PLATINO Team. Sex-related differences in COPD in five Latin American cities: the PLATINO study. Eur Respir J 2010;36:1034-1041.
20. Kanervisto M, Vasankari T, Laitinen T, Heliövaara M, Jousilahti P, Saarelainen S. Low socioeconomic status is associated with chronic obstructive airway diseases. Respir Med 2011;105:1140-1146.
21. Yin P, Zhang M, Li Y, Jiang Y, Zhao W. Prevalence of COPD and its association with socioeconomic status in China: findings from China Chronic Disease Risk Factor Surveillance 2007. BMC Public Health 2011;11:586.
22. Bardach A, Perdomo HA, Gándara RA, Ciapponi A. [Income and smoking prevalence in Latin America: a systematic review and meta-analysis]. Rev Panam Salud Publica 2016;40:263-271. Spanish.
23. Kim JD, Seo JH, Shin YJ, Kim CY. The factors associated with smoking behavior of low-income people. Health Soc Welfare Rev 2013;33:577-602.
24. Zysman M, Raherison-Semjen C. Women's COPD. Front Med (Lausanne) 2022;8:600107.
25. Hagstad S, Bjerg A, Ekerljung L, et al. Passive smoking exposure is associated with increased risk of COPD in never smokers. Chest 2014;145:1298-1304.

https://doi.org/10.3904/kjim.2023.036

26. Kurmi OP, Semple S, Simkhada P, Smith WC, Ayres JG. COPD and chronic bronchitis risk of indoor air pollution from solid fuel: a systematic review and meta-analysis. Thorax 2010;65:221-228.
27. Hu G, Zhou Y, Tian J, et al. Risk of COPD from exposure to biomass smoke: a metaanalysis. Chest 2010;138:20-31.
28. Hong Y, Lim MN, Kim WJ, et al. Influence of environmental exposures on patients with chronic obstructive pulmonary disease in Korea. Tuberc Respir Dis (Seoul) 2014;76:226-232.
29. Malhotra J, Malvezzi M, Negri E, La Vecchia C, Boffetta P. Risk factors for lung cancer worldwide. Eur Respir J 2016;48:889-902.
30. Rodriguez-Lara V, Avila-Costa MR. An overview of lung cancer in women and the impact of estrogen in lung carcinogenesis and lung cancer treatment. Front Med (Lausanne) 2021;8:600121.
31. de-Torres JP, Wilson DO, Sanchez-Salcedo P, et al. Lung cancer in patients with chronic obstructive pulmonary disease. Development and validation of the COPD Lung Cancer Screening Score. Am J Respir Crit Care Med 2015;191:285-291.
32. Park HY, Kang D, Shin SH, et al. Chronic obstructive pulmonary disease and lung cancer incidence in never smokers: a cohort study. Thorax 2020;75:506-509.
33. Nagasaka M, Lehman A, Chlebowski R, et al. COPD and lung cancer incidence in the Women's Health Initiative Observational Study: a brief report. Lung Cancer 2020;141:78-81.
34. Bade BC, Dela Cruz CS. Lung cancer 2020: epidemiology, etiology, and prevention. Clin Chest Med 2020;41:1-24.
35. Ortega-Gómez A, Rangel-Escareño C, Molina-Romero C, et al. Gene-expression profiles in lung adenocarcinomas related to chronic wood smoke or tobacco exposure. Respir Res 2016;17:42.
36. Mannino DM, Aguayo SM, Petty TL, Redd SC. Low lung function and incident lung cancer in the United States: data From the First National Health and Nutrition Examination Survey follow-up. Arch Intern Med 2003;163:1475-1480.
37. de Torres JP, Marín JM, Casanova C, et al. Lung cancer in patients with chronic obstructive pulmonary disease-- incidence and predicting factors. Am J Respir Crit Care Med 2011;184:913-919.
38. Kang HS, Park YM, Ko SH, et al. Impaired lung function and lung cancer incidence: a nationwide population-based cohort study. J Clin Med 2022;11:1077.
39. Schottenfeld D, Beebe-Dimmer JL. Advances in cancer epidemiology: understanding causal mechanisms and the evidence for implementing interventions. Annu Rev Public Health 2005;26:37-60.

Received : January 25, 2023
Revised : July 14, 2023
Accepted : October 19, 2023

Correspondence to
Jae-Yeol Kim, M.D., Ph.D.
Department of Internal Medicine, Chung-Ang University Hospital, Chung-Ang University College of Medicine, 102, Heukseok-ro, Dongjak-gu, Seoul 06973, Korea
Tel: +82-2-6299-1396, Fax: +82-2-6299-2017
E-mail: jykimmd@cau.ac.kr
https://orcid.org/0000-0003-3631-4610

CRedit authorship contributions
Moon Seong Baek: conceptualization, data curation, methodology, writing - original draft, writing - review & editing; Haegwang Shin: data curation, formal analysis, writing - original draft, writing - review & editing; Kang-Mo Gu: data curation; Hae In Jung: data curation; Won Young Kim: data curation; Jae-Woo Jung: data curation, formal analysis, methodology; Jong-Wook Shin: data curation; Sun-Young Jung: formal analysis, methodology; Jae Yeol Kim: conceptualization, project administration, writing - original draft, writing - review & editing

Conflicts of interest
The authors disclose no conflicts.

Funding
None

Availability of data and materials
The dataset used and analyzed in this study is available from the corresponding author upon reasonable request.